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May 31, 2011

Via ECF and First Class Mail
The Honorable Madeline Cox Arleo
United States Magistrate Judge
M.L. King, Jr. Federal Bldg. & Courthouse, Room 2060
50 Walnut Street
Newark, New Jersey 07102

Re: *Jazz Pharmaceuticals, Inc. v. Roxane Laboratories, Inc.*
Civil Action No. 2:10-cv-06108 (SDW)(MCA)

Dear Judge Arleo:

We along with Locke Lord Bissell & Liddell LLP represent defendant Roxane Laboratories, Inc. ("Roxane") in the above captioned action. We write in advance of the June 6, 2011 conference regarding the disputed Discovery Confidentiality Order, and in response to plaintiff's letter of May 16, 2011. (*see* D.I. #29).

As an initial matter, we were surprised to have received plaintiff's May 16, 2011 letter as the parties had not met and conferred on the issues raised therein. As is evident from the correspondence exchanged between the parties and discussed below, plaintiff has not been negotiating in good faith with Roxane. Indeed, Roxane had been waiting for a response from plaintiff regarding the scheduling order issues and the parties had scheduled and met and conferred on the issues relating to the production of samples from third-party Norac, Inc. on May 18 and 25.

Roxane would also like to offer additional support for its request for a patent prosecution bar in the Discovery Confidentiality Order, which is scheduled for oral argument on June 6, 2011.

I. Discovery Confidentiality Order

Further to our position stated in the parties' March 29, 2011 submission to your honor (D.I. #26), Roxane submits for Your Honor's consideration, a provision of the Biologics Price Competition and Innovation Act of 2009 ("BPCIA"), which parallels the Hatch-Waxman provisions for facilitating approval of generic drugs. The BPCIA creates a new pathway for the approval of biological products shown to be biosimilar to, or interchangeable with, a biological reference product. *See* 42 U.S.C § 262. One of the procedures set forth in the BPCIA relates to the transfer of confidential information from the applicant for the biosimilar product (equivalent to the ANDA applicant in the Hatch-Waxman context or Roxane in this action) to the reference product sponsor (equivalent to the NDA holder in the Hatch-Waxman context or plaintiff in this action). Congress included in the BPCIA confidentiality procedures, a provision requiring a patent prosecution bar for both the outside and in-house counsel of the biological reference product sponsor, specifically mandating that "such attorney does not engage, formally or informally, in patent prosecution relevant or related to the reference product." (*See* Ex. A, 42 USC § 262(l)(B)(ii).) Roxane respectfully submits that consistent with the Federal Circuit's recognition in the *In re Deutsche Bank* case, Congress also recognized that information to be exchanged between the reference drug sponsor/NDA-applicant or plaintiff in this action and the biosimilar product applicant/ANDA-applicant or Roxane in this action is so "potentially confidential" and sensitive as to warrant a patent prosecution bar.

This is especially true here where plaintiff is continuing to aggressively prosecute its patent applications before the United States Patent Office in an attempt to create additional claims that are highly relevant to the instant action. (*See* Ex. B, Jan. 10, 2011 Preliminary Amendment to Application No. 12/913,644 (seeking claims to a method of dosing sodium oxybate in another application that claims priority to the same provisional application that U.S. Patent Nos. 6,472,431, 6,780,889, 7,262,219, and 7,851,506, all at issue in this case).) Indeed, plaintiff recently filed its third complaint asserting its newly-issued eighth patent (U.S. Patent No. 7,895,059 ("the '059 patent")) against Roxane, initiating Civil Action No. 11-2523. The '059 patent is part of the same patent family as three of the other patents-in-suit (U.S. Patent Nos. 7,668,730; 7,765,106 and 7,765,107), and accordingly, Roxane submits that this new suit should be consolidated with the present action. As further evidence of plaintiff's aggressive patent prosecution tactics, plaintiff filed yet another continuation application based on the '059 patent, which plaintiff continues to prosecute while the current lawsuit progresses, presumably so that plaintiff can file additional lawsuits against Roxane as the case proceeds.

Accordingly, and as stated in the parties' March 29, 2011 letter to the Court, more than good cause exists to require the patent prosecution bar proposed by Roxane.

II. Proposed Scheduling Order

As directed by the Court on the March 22, 2011 teleconference, the parties had been conferring to reach an agreement regarding the proposed scheduling order and successfully resolved a number of disputes. Hence, the surprise when plaintiff unilaterally cutoff further negotiation and submitted its May 16th letter to the Court. Plaintiff's May 16th letter fails to apprise the Court that while the parties did initially disagree as to whether three rounds of expert reports were indeed necessary, Roxane, in the spirit of compromise offered an exchange—Roxane would agree to a schedule that contemplates exchanging three rounds of expert reports as plaintiff proposes, in exchange for resolving the one other remaining issue regarding the scheduling order – Roxane's request to include in the proposed scheduling order proposed dates for the pretrial conference (October 22, 2012) and trial (December 10, 2012). (*See* Ex. C, Apr. 29, 2011 Goodin letter to Brier at 2.) Plaintiff never responded to Roxane's offer and instead submitted its May 16, 2011 letter to the Court. In other words, there was no formal meet and confer on this issue before plaintiff decided to submit its letter to the Court.

As stated in Roxane's April 29, 2011 letter, Roxane initially disagreed with plaintiff's proposal for three rounds of expert reports because it would needlessly lengthen the time required to be trial ready. Under Roxane's two-round expert report proposal, both parties would have submitted reports on the issues each party bears the burden of proving at trial, such that plaintiff would submit any expert report(s) on the issue of secondary considerations of nonobviousness during the first round and plaintiff would still have the opportunity to respond to Roxane's expert(s)' opinions on invalidity—including the scope of the prior art—during the second round of expert reports. Plaintiff argues that it is entitled to see Roxane's invalidity case in expert reports before offering a report on secondary considerations. As plaintiff well knows, however, the factors of secondary considerations of nonobviousness set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966) are not related to or dependent on the state of the prior art, such that plaintiff should be able to prepare its reports on secondary considerations without seeing Roxane's invalidity case in expert reports. Plaintiff will have been fully apprised of Roxane's invalidity contentions, and are already in possession of Roxane's preliminary contentions. In fact, Magistrate Judge Falk and Judge Cavanaugh agreed with Roxane's proposed expert exchange procedure in another Hatch-Waxman case and required plaintiff in that action to submit any expert report(s) on secondary considerations during the first of two rounds of expert reports. (*See* Ex. D, D.I. 266, Nov. 20, 2008 Amendment to Pretrial Scheduling Order in *Eli Lilly and Company v. Actavis Elizabeth LLC, et al.*, Civil Action No. 07-3770 (DMC) (MF).)

Nevertheless, in an effort not to burden the Court with a simple scheduling issue, Roxane agreed to plaintiff's three rounds of expert reports proposal, provided that plaintiff would agree to include proposed dates for the pretrial conference (October 22, 2012) and for trial (December

10, 2012) in the scheduling order. (*See* Ex. C. at 2.) The 30-month stay of FDA approval of Roxane's ANDA expires in April 2013 and the dates that Roxane proposed would give Judge Wigenton sufficient time to issue an opinion following trial. Because the parties did not meet and confer on this issue, Roxane again does not understand why plaintiff is not agreeable to inserting proposed dates for the pretrial conference and trial that would allow for the case to be resolved before the 30-month stay expires.

For the reasons stated above, Roxane respectfully requests that the Court enter Roxane's proposed pretrial schedule, attached hereto as Exhibit E.

III. Roxane's (and third-party Norac's) Confidential Documents and Information

Again, the parties had not met and conferred on this issue before plaintiff submitted its letter to the Court. Roxane respectfully submits that both Roxane and Norac are justified in requiring entry of a Discovery Confidential Order before producing highly confidential, commercially-sensitive, and trade-secret information. While Roxane believes that plaintiff has sufficient information to submit a response to Roxane's noninfringement (and invalidity) contentions, which Roxane timely served on plaintiff, Roxane would not necessarily be opposed to a short extension for plaintiff to submit its infringement contentions, so long as it does not affect any of the other dates in the proposed scheduling order that have been agreed upon by the parties, *i.e.*, proposed dates 1, 3-14 and 16 of plaintiff's proposed schedule attached to plaintiff's letter as Exhibit A and proposed dates 1, 3-14 and 16 of Roxane's proposed schedule, attached hereto as Exhibit E.

Moreover, plaintiff's request that this Court order Norac to produce samples appears to be misplaced. Norac is not subject to the jurisdiction of this Court, but instead was subpoenaed for information based on a subpoena issued out of the Central District of California. Accordingly, any recourse against Norac that Jazz might have needs to be requested from that court. *See Highland Tank & Mfg. Co. v. PS Int'l, Inc.*, 227 F.R.D. 374, 380-81 (E.D. Pa. 2005 (*citing Fincher v. Keller Industries, Inc.*, 129 F.R.D. 123, 125 (M.D.N.C. 1990)).

Finally, Roxane is at a loss as to how Jazz continues to complain about Roxane meeting its discovery obligations when Roxane has already provided plaintiff with its complete ANDA, noninfringement and invalidity contentions. Moreover, third-party Norac has also provided plaintiff with the complete DMF referenced in Roxane's ANDA and a multitude of other documents. Plaintiff, on the other hand, has yet to provide Roxane with any documents and now seeks to delay its obligations to submit its infringement contentions and even identify the claims it seeks to assert against Roxane. The discovery process is not a one-sided affair, with defendant providing all of its information and plaintiff providing nothing. Indeed, Roxane will

address plaintiff's shirking of its discovery obligations in a separate letter to Your Honor shortly so that it can be addressed at the June status conference.

Respectfully submitted,

Theodora McCormick

cc: All Counsel of Record (via ECF)

EXHIBIT A

42 U.S.C. 262 Regulation of biological products

TITLE 42--THE PUBLIC HEALTH AND WELFARE
CHAPTER 6A--PUBLIC HEALTH SERVICE
SUBCHAPTER II--GENERAL POWERS AND DUTIES
Part F--Licensing of Biological Products and Clinical Laboratories
subpart 1--biological products

§ 262. Regulation of biological products

(a) Introduction of biological products into interstate commerce; requirements; exemption.

(1) No person shall introduce or deliver for introduction into interstate commerce any biological product unless--

(A) a biologics license under this subsection or subsection (k) is in effect for the biological product; and

(B) each package of the biological product is plainly marked with--

(i) the proper name of the biological product contained in the package;

(ii) the name, address, and applicable license number of the manufacturer of the biological product; and

(iii) the expiration date of the biological product.

(2) (A) The Secretary shall establish, by regulation, requirements for the approval, suspension, and revocation of biologics licenses.

(B) The Secretary shall approve a biologics license application--

(i) on the basis of a demonstration that--

(I) the biological product that is the subject of the application is safe, pure, and potent; and

(II) the facility in which the biological product is manufactured, processed, packed, or held meets standards designed to assure that the biological product continues to be safe, pure, and potent; and

(ii) if the applicant (or other appropriate person) consents to the inspection of the facility that is the subject of the application, in accordance with subsection (c).

(3) The Secretary shall prescribe requirements under which a biological product undergoing investigation shall be exempt from the requirements of paragraph (1).

(b) Falsely labeling or marking package or container; altering label or mark No person shall falsely label or mark any package or container of any biological product or alter any label or mark on the package or container of the biological product so as to falsify the label or mark.

(c) Inspection of establishment for propagation and preparation Any officer, agent, or employee of the Department of Health and Human Services, authorized by the Secretary for the purpose, may during all reasonable hours enter and inspect any establishment for the propagation or manufacture and preparation of any biological product.

(d) Recall of product presenting imminent hazard; violations

(1) Upon a determination that a batch, lot, or other quantity of a product licensed under this

section presents an imminent or substantial hazard to the public health, the Secretary shall issue an order immediately ordering the recall of such batch, lot, or other quantity of such product. An order under this paragraph shall be issued in accordance with section 554 of title 5.

(2) Any violation of paragraph (1) shall subject the violator to a civil penalty of up to $100,000 per day of violation. The amount of a civil penalty under this paragraph shall, effective December 1 of each year beginning 1 year after the effective date of this paragraph, be increased by the percent change in the Consumer Price Index for the base quarter of such year over the Consumer Price Index for the base quarter of the preceding year, adjusted to the nearest \1/10\ of 1 percent. For purposes of this paragraph, the term ``base quarter'', as used with respect to a year, means the calendar quarter ending on September 30 of such year and the price index for a base quarter is the arithmetical mean of such index for the 3 months comprising such quarter.

(e) Interference with officers No person shall interfere with any officer, agent, or employee of the Service in the performance of any duty imposed upon him by this section or by regulations made by authority thereof.

(f) Penalties for offenses Any person who shall violate, or aid or abet in violating, any of the provisions of this section shall be punished upon conviction by a fine not exceeding $500 or by imprisonment not exceeding one year, or by both such fine and imprisonment, in the discretion of the court.

(g) Construction with other laws. Nothing contained in this chapter shall be construed as in any way affecting, modifying, repealing, or superseding the provisions of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 301 et seq.].

(h) Exportation of partially processed biological products

A partially processed biological product which--

(1) is not in a form applicable to the prevention, treatment, or cure of diseases or injuries of man;

(2) is not intended for sale in the United States; and

(3) is intended for further manufacture into final dosage form outside the United States,

shall be subject to no restriction on the export of the product under this chapter or the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 301 et. seq.] if the product is manufactured, processed, packaged, and held in conformity with current good manufacturing practice requirements or meets international manufacturing standards as certified by an international standards organization recognized by the Secretary and meets the requirements of section 801(e)(1) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 381(e)).

(i) Biological product defined. In this section:

(1) the term “biological product” means a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein (except any chemically synthesized polypeptide)or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of a disease or condition of human beings.

(2) The term 'biosimilar' or 'biosimilarity', in reference to a biological product that is the subject of an application under subsection (k), means--

(A) that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components; and

(B) there are no clinically meaningful differences between the biological product and

the reference product in terms of the safety, purity, and potency of the product.

(3) The term 'interchangeable' or 'interchangeability', in reference to a biological product that is shown to meet the standards described in subsection (k)(4), means that the biological product may be substituted for the reference product without the intervention of the health care provider who prescribed the reference product.

(4) The term 'reference product' means the single biological product licensed under subsection (a) against which a biological product is evaluated in an application submitted under subsection (k).

(j) Application of other law. The Federal Food, Drug, and Cosmetic Act [21 USCS §§ 301 et seq.] applies to a biological product subject to regulation under this section, except that a product for which a license has been approved under subsection (a) shall not be required to have an approved application under section 505 of such Act [21 USCS § 355].

(k) Licensure of Biological Products as Biosimilar or Interchangeable-

(1) **IN GENERAL**- Any person may submit an application for licensure of a biological product under this subsection.

(2) **CONTENT**-

(A) **IN GENERAL**-

(i) **REQUIRED INFORMATION**- An application submitted under this subsection shall include information demonstrating that--

(I) the biological product is biosimilar to a reference product based upon data derived from--

(aa) analytical studies that demonstrate that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components;

(bb) animal studies (including the assessment of toxicity); and

(cc) a clinical study or studies (including the assessment of immunogenicity and pharmacokinetics or pharmacodynamics) that are sufficient to demonstrate safety, purity, and potency in 1 or more appropriate conditions of use for which the reference product is licensed and intended to be used and for which licensure is sought for the biological product;

(II) the biological product and reference product utilize the same mechanism or mechanisms of action for the condition or conditions of use prescribed, recommended, or suggested in the proposed labeling, but only to the extent the mechanism or mechanisms of action are known for the reference product;

(III) the condition or conditions of use prescribed, recommended, or suggested in the labeling proposed for the biological product have been previously approved for the reference product;

(IV) the route of administration, the dosage form, and the strength of the biological product are the same as those of the reference product; and

(V) the facility in which the biological product is manufactured, processed, packed, or held meets standards designed to assure that the biological product continues to be safe, pure, and potent.

(ii) **DETERMINATION BY SECRETARY**- The Secretary may determine, in the Secretary's discretion, that an element described in clause (i)(I) is unnecessary in

an application submitted under this subsection.

(iii) **ADDITIONAL INFORMATION**- An application submitted under this subsection--

(I) shall include publicly-available information regarding the Secretary's previous determination that the reference product is safe, pure, and potent; and

(II) may include any additional information in support of the application, including publicly-available information with respect to the reference product or another biological product.

(B) **INTERCHANGEABILITY**- An application (or a supplement to an application) submitted under this subsection may include information demonstrating that the biological product meets the standards described in paragraph (4).

(3) **EVALUATION BY SECRETARY**- Upon review of an application (or a supplement to an application) submitted under this subsection, the Secretary shall license the biological product under this subsection if--

(A) the Secretary determines that the information submitted in the application (or the supplement) is sufficient to show that the biological product--

(i) is biosimilar to the reference product; or

(ii) meets the standards described in paragraph (4), and therefore is interchangeable with the reference product; and

(B) the applicant (or other appropriate person) consents to the inspection of the facility that is the subject of the application, in accordance with subsection (c).

(4) **SAFETY STANDARDS FOR DETERMINING INTERCHANGEABILITY**- Upon review of an application submitted under this subsection or any supplement to such application, the Secretary shall determine the biological product to be interchangeable with the reference product if the Secretary determines that the information submitted in the application (or a supplement to such application) is sufficient to show that--

(A) the biological product--

(i) is biosimilar to the reference product; and

(ii) can be expected to produce the same clinical result as the reference product in any given patient; and

(B) for a biological product that is administered more than once to an individual, the risk in terms of safety or diminished efficacy of alternating or switching between use of the biological product and the reference product is not greater than the risk of using the reference product without such alternation or switch.

(5) **GENERAL RULES**-

(A) **ONE REFERENCE PRODUCT PER APPLICATION**- A biological product, in an application submitted under this subsection, may not be evaluated against more than 1 reference product.

(B) **REVIEW**- An application submitted under this subsection shall be reviewed by the division within the Food and Drug Administration that is responsible for the review and approval of the application under which the reference product is licensed.

(C) **RISK EVALUATION AND MITIGATION STRATEGIES**- The authority of the Secretary with respect to risk evaluation and mitigation strategies under the Federal Food, Drug, and Cosmetic Act shall apply to biological products licensed under this subsection in the same manner as such authority applies to biological products licensed under subsection (a).

(6) **EXCLUSIVITY FOR FIRST INTERCHANGEABLE BIOLOGICAL PRODUCT**- Upon review of an application submitted under this subsection relying on the same reference product for which a prior biological product has received a determination of interchangeability for any condition of use, the Secretary shall not make a determination under paragraph (4) that the second or subsequent biological product is interchangeable for any condition of use until the earlier of--

(A) 1 year after the first commercial marketing of the first interchangeable biosimilar biological product to be approved as interchangeable for that reference product;

(B) 18 months after--

(i) a final court decision on all patents in suit in an action instituted under subsection (l)(6) against the applicant that submitted the application for the first approved interchangeable biosimilar biological product; or

(ii) the dismissal with or without prejudice of an action instituted under subsection (l)(6) against the applicant that submitted the application for the first approved interchangeable biosimilar biological product; or

(C)(i) 42 months after approval of the first interchangeable biosimilar biological product if the applicant that submitted such application has been sued under subsection (l)(6) and such litigation is still ongoing within such 42-month period; or

(ii) 18 months after approval of the first interchangeable biosimilar biological product if the applicant that submitted such application has not been sued under subsection (l)(6).

For purposes of this paragraph, the term final court decision' means a final decision of a court from which no appeal (other than a petition to the United States Supreme Court for a writ of certiorari) has been or can be taken.

(7) **EXCLUSIVITY FOR REFERENCE PRODUCT-**

(A) **EFFECTIVE DATE OF BIOSIMILAR APPLICATION APPROVAL**- Approval of an application under this subsection may not be made effective by the Secretary until the date that is 12 years after the date on which the reference product was first licensed under subsection (a).

(B) **FILING PERIOD**- An application under this subsection may not be submitted to the Secretary until the date that is 4 years after the date on which the reference product was first licensed under subsection (a).

(C) **FIRST LICENSURE**- Subparagraphs (A) and (B) shall not apply to a license for or approval of--

(i) a supplement for the biological product that is the reference product; or

(ii) a subsequent application filed by the same sponsor or manufacturer of the biological product that is the reference product (or a licensor, predecessor in interest, or other related entity) for--

(I) a change (not including a modification to the structure of the biological product) that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device, or strength; or

(II) a modification to the structure of the biological product that does not result in a change in safety, purity, or potency.

(8) **GUIDANCE DOCUMENTS-**

(A) **IN GENERAL**- The Secretary may, after opportunity for public comment, issue guidance in accordance, except as provided in subparagraph (B)(i), with section 701(h)

of the Federal Food, Drug, and Cosmetic Act with respect to the licensure of a biological product under this subsection. Any such guidance may be general or specific.

(B) **PUBLIC COMMENT**-

(i) **IN GENERAL**- The Secretary shall provide the public an opportunity to comment on any proposed guidance issued under subparagraph (A) before issuing final guidance.

(ii) **INPUT REGARDING MOST VALUABLE GUIDANCE**- The Secretary shall establish a process through which the public may provide the Secretary with input regarding priorities for issuing guidance.

(C) **NO REQUIREMENT FOR APPLICATION CONSIDERATION**- The issuance (or non-issuance) of guidance under subparagraph (A) shall not preclude the review of, or action on, an application submitted under this subsection.

(D) **REQUIREMENT FOR PRODUCT CLASS-SPECIFIC GUIDANCE**- If the Secretary issues product class-specific guidance under subparagraph (A), such guidance shall include a description of--

(i) the criteria that the Secretary will use to determine whether a biological product is highly similar to a reference product in such product class; and

(ii) the criteria, if available, that the Secretary will use to determine whether a biological product meets the standards described in paragraph (4).

(E) **CERTAIN PRODUCT CLASSES**-

(i) **GUIDANCE**- The Secretary may indicate in a guidance document that the science and experience, as of the date of such guidance, with respect to a product or product class (not including any recombinant protein) does not allow approval of an application for a license as provided under this subsection for such product or product class.

(ii) **MODIFICATION OR REVERSAL**- The Secretary may issue a subsequent guidance document under subparagraph (A) to modify or reverse a guidance document under clause (i).

(iii) **NO EFFECT ON ABILITY TO DENY LICENSE**- Clause (i) shall not be construed to require the Secretary to approve a product with respect to which the Secretary has not indicated in a guidance document that the science and experience, as described in clause (i), does not allow approval of such an application.

(l) Patents-

(1) **CONFIDENTIAL ACCESS TO SUBSECTION (k) APPLICATION**-

(A) **APPLICATION OF PARAGRAPH**- Unless otherwise agreed to by a person that submits an application under subsection (k) (referred to in this subsection as the 'subsection (k) applicant') and the sponsor of the application for the reference product (referred to in this subsection as the 'reference product sponsor'), the provisions of this paragraph shall apply to the exchange of information described in this subsection.

(B) **IN GENERAL**-

(i) **PROVISION OF CONFIDENTIAL INFORMATION**- When a subsection (k) applicant submits an application under subsection (k), such applicant shall provide to the persons described in clause (ii), subject to the terms of this paragraph, confidential access to the information required to be produced pursuant to paragraph (2) and any other information that the subsection (k) applicant determines, in its sole discretion, to be appropriate (referred to in this subsection as the 'confidential

information').

(ii) **RECIPIENTS OF INFORMATION**- The persons described in this clause are the following:

(I) **OUTSIDE COUNSEL**- One or more attorneys designated by the reference product sponsor who are employees of an entity other than the reference product sponsor (referred to in this paragraph as the 'outside counsel'), provided that such attorneys do not engage, formally or informally, in patent prosecution relevant or related to the reference product.

(II) **IN-HOUSE COUNSEL**- One attorney that represents the reference product sponsor who is an employee of the reference product sponsor, provided that such attorney does not engage, formally or informally, in patent prosecution relevant or related to the reference product.

(iii) **PATENT OWNER ACCESS**- A representative of the owner of a patent exclusively licensed to a reference product sponsor with respect to the reference product and who has retained a right to assert the patent or participate in litigation concerning the patent may be provided the confidential information, provided that the representative informs the reference product sponsor and the subsection (k) applicant of his or her agreement to be subject to the confidentiality provisions set forth in this paragraph, including those under clause (ii).

(C) **LIMITATION ON DISCLOSURE**- No person that receives confidential information pursuant to subparagraph (B) shall disclose any confidential information to any other person or entity, including the reference product sponsor employees, outside scientific consultants, or other outside counsel retained by the reference product sponsor, without the prior written consent of the subsection (k) applicant, which shall not be unreasonably withheld.

(D) **USE OF CONFIDENTIAL INFORMATION**- Confidential information shall be used for the sole and exclusive purpose of determining, with respect to each patent assigned to or exclusively licensed by the reference product sponsor, whether a claim of patent infringement could reasonably be asserted if the subsection (k) applicant engaged in the manufacture, use, offering for sale, sale, or importation into the United States of the biological product that is the subject of the application under subsection (k).

(E) **OWNERSHIP OF CONFIDENTIAL INFORMATION**- The confidential information disclosed under this paragraph is, and shall remain, the property of the subsection (k) applicant. By providing the confidential information pursuant to this paragraph, the subsection (k) applicant does not provide the reference product sponsor or the outside counsel any interest in or license to use the confidential information, for purposes other than those specified in subparagraph (D).

(F) **EFFECT OF INFRINGEMENT ACTION**- In the event that the reference product sponsor files a patent infringement suit, the use of confidential information shall continue to be governed by the terms of this paragraph until such time as a court enters a protective order regarding the information. Upon entry of such order, the subsection (k) applicant may redesignate confidential information in accordance with the terms of that order. No confidential information shall be included in any publicly-available complaint or other pleading. In the event that the reference product sponsor does not file an infringement action by the date specified in paragraph (6), the reference product sponsor shall return or destroy all confidential information received under this paragraph, provided that if the reference product sponsor opts to destroy such information, it will confirm destruction in writing to the subsection (k) applicant.

(G) **RULE OF CONSTRUCTION**- Nothing in this paragraph shall be construed--

(i) as an admission by the subsection (k) applicant regarding the validity, enforceability, or infringement of any patent; or

(ii) as an agreement or admission by the subsection (k) applicant with respect to the competency, relevance, or materiality of any confidential information.

(H) **EFFECT OF VIOLATION**- The disclosure of any confidential information in violation of this paragraph shall be deemed to cause the subsection (k) applicant to suffer irreparable harm for which there is no adequate legal remedy and the court shall consider immediate injunctive relief to be an appropriate and necessary remedy for any violation or threatened violation of this paragraph.

(2) **SUBSECTION (k) APPLICATION INFORMATION**- Not later than 20 days after the Secretary notifies the subsection (k) applicant that the application has been accepted for review, the subsection (k) applicant--

(A) shall provide to the reference product sponsor a copy of the application submitted to the Secretary under subsection (k), and such other information that describes the process or processes used to manufacture the biological product that is the subject of such application; and

(B) may provide to the reference product sponsor additional information requested by or on behalf of the reference product sponsor.

(3) **LIST AND DESCRIPTION OF PATENTS**-

(A) **LIST BY REFERENCE PRODUCT SPONSOR**- Not later than 60 days after the receipt of the application and information under paragraph (2), the reference product sponsor shall provide to the subsection (k) applicant--

(i) a list of patents for which the reference product sponsor believes a claim of patent infringement could reasonably be asserted by the reference product sponsor, or by a patent owner that has granted an exclusive license to the reference product sponsor with respect to the reference product, if a person not licensed by the reference product sponsor engaged in the making, using, offering to sell, selling, or importing into the United States of the biological product that is the subject of the subsection (k) application; and

(ii) an identification of the patents on such list that the reference product sponsor would be prepared to license to the subsection (k) applicant.

(B) **LIST AND DESCRIPTION BY SUBSECTION (k) APPLICANT**- Not later than 60 days after receipt of the list under subparagraph (A), the subsection (k) applicant--

(i) may provide to the reference product sponsor a list of patents to which the subsection (k) applicant believes a claim of patent infringement could reasonably be asserted by the reference product sponsor if a person not licensed by the reference product sponsor engaged in the making, using, offering to sell, selling, or importing into the United States of the biological product that is the subject of the subsection (k) application;

(ii) shall provide to the reference product sponsor, with respect to each patent listed by the reference product sponsor under subparagraph (A) or listed by the subsection (k) applicant under clause (i)--

(I) a detailed statement that describes, on a claim by claim basis, the factual and legal basis of the opinion of the subsection (k) applicant that such patent is invalid, unenforceable, or will not be infringed by the commercial marketing of the biological product that is the subject of the subsection (k) application; or

(II) a statement that the subsection (k) applicant does not intend to begin commercial marketing of the biological product before the date that such patent expires; and

(iii) shall provide to the reference product sponsor a response regarding each patent identified by the reference product sponsor under subparagraph (A)(ii).

(C) **DESCRIPTION BY REFERENCE PRODUCT SPONSOR**- Not later than 60 days after receipt of the list and statement under subparagraph (B), the reference product sponsor shall provide to the subsection (k) applicant a detailed statement that describes, with respect to each patent described in subparagraph (B)(ii)(I), on a claim by claim basis, the factual and legal basis of the opinion of the reference product sponsor that such patent will be infringed by the commercial marketing of the biological product that is the subject of the subsection (k) application and a response to the statement concerning validity and enforceability provided under subparagraph (B)(ii)(I).

(4) **PATENT RESOLUTION NEGOTIATIONS**-

(A) **IN GENERAL**- After receipt by the subsection (k) applicant of the statement under paragraph (3)(C), the reference product sponsor and the subsection (k) applicant shall engage in good faith negotiations to agree on which, if any, patents listed under paragraph (3) by the subsection (k) applicant or the reference product sponsor shall be the subject of an action for patent infringement under paragraph (6).

(B) **FAILURE TO REACH AGREEMENT**- If, within 15 days of beginning negotiations under subparagraph (A), the subsection (k) applicant and the reference product sponsor fail to agree on a final and complete list of which, if any, patents listed under paragraph (3) by the subsection (k) applicant or the reference product sponsor shall be the subject of an action for patent infringement under paragraph (6), the provisions of paragraph (5) shall apply to the parties.

(5) **PATENT RESOLUTION IF NO AGREEMENT**-

(A) **NUMBER OF PATENTS**- The subsection (k) applicant shall notify the reference product sponsor of the number of patents that such applicant will provide to the reference product sponsor under subparagraph (B)(i)(I).

(B) **EXCHANGE OF PATENT LISTS**-

(i) **IN GENERAL**- On a date agreed to by the subsection (k) applicant and the reference product sponsor, but in no case later than 5 days after the subsection (k) applicant notifies the reference product sponsor under subparagraph (A), the subsection (k) applicant and the reference product sponsor shall simultaneously exchange--

(I) the list of patents that the subsection (k) applicant believes should be the subject of an action for patent infringement under paragraph (6); and

(II) the list of patents, in accordance with clause (ii), that the reference product sponsor believes should be the subject of an action for patent infringement under paragraph (6).

(ii) **NUMBER OF PATENTS LISTED BY REFERENCE PRODUCT SPONSOR**-

(I) **IN GENERAL**- Subject to subclause (II), the number of patents listed by the reference product sponsor under clause (i)(II) may not exceed the number of patents listed by the subsection (k) applicant under clause (i)(I).

(II) **EXCEPTION**- If a subsection (k) applicant does not list any patent under clause (i)(I), the reference product sponsor may list 1 patent under clause (i)(II).

(6) **IMMEDIATE PATENT INFRINGEMENT ACTION**-

(A) **ACTION IF AGREEMENT ON PATENT LIST**- If the subsection (k) applicant and the reference product sponsor agree on patents as described in paragraph (4), not later than 30 days after such agreement, the reference product sponsor shall bring an action for patent infringement with respect to each such patent.

(B) **ACTION IF NO AGREEMENT ON PATENT LIST**- If the provisions of paragraph (5) apply to the parties as described in paragraph (4)(B), not later than 30 days after the exchange of lists under paragraph (5)(B), the reference product sponsor shall bring an action for patent infringement with respect to each patent that is included on such lists.

(C) **NOTIFICATION AND PUBLICATION OF COMPLAINT**-

(i) **NOTIFICATION TO SECRETARY**- Not later than 30 days after a complaint is served to a subsection (k) applicant in an action for patent infringement described under this paragraph, the subsection (k) applicant shall provide the Secretary with notice and a copy of such complaint.

(ii) **PUBLICATION BY SECRETARY**- The Secretary shall publish in the Federal Register notice of a complaint received under clause (i).

(7) **NEWLY ISSUED OR LICENSED PATENTS**- In the case of a patent that--

(A) is issued to, or exclusively licensed by, the reference product sponsor after the date that the reference product sponsor provided the list to the subsection (k) applicant under paragraph (3)(A); and

(B) the reference product sponsor reasonably believes that, due to the issuance of such patent, a claim of patent infringement could reasonably be asserted by the reference product sponsor if a person not licensed by the reference product sponsor engaged in the making, using, offering to sell, selling, or importing into the United States of the biological product that is the subject of the subsection (k) application,

not later than 30 days after such issuance or licensing, the reference product sponsor shall provide to the subsection (k) applicant a supplement to the list provided by the reference product sponsor under paragraph (3)(A) that includes such patent, not later than 30 days after such supplement is provided, the subsection (k) applicant shall provide a statement to the reference product sponsor in accordance with paragraph (3)(B), and such patent shall be subject to paragraph (8).

(8) **NOTICE OF COMMERCIAL MARKETING AND PRELIMINARY INJUNCTION**-

(A) **NOTICE OF COMMERCIAL MARKETING**- The subsection (k) applicant shall provide notice to the reference product sponsor not later than 180 days before the date of the first commercial marketing of the biological product licensed under subsection (k).

(B) **PRELIMINARY INJUNCTION**- After receiving the notice under subparagraph (A) and before such date of the first commercial marketing of such biological product, the reference product sponsor may seek a preliminary injunction prohibiting the subsection (k) applicant from engaging in the commercial manufacture or sale of such biological product until the court decides the issue of patent validity, enforcement, and infringement with respect to any patent that is--

(i) included in the list provided by the reference product sponsor under paragraph (3)(A) or in the list provided by the subsection (k) applicant under paragraph (3)(B); and

(ii) not included, as applicable, on--

(I) the list of patents described in paragraph (4); or

(II) the lists of patents described in paragraph (5)(B).

(C) **REASONABLE COOPERATION**- If the reference product sponsor has sought a preliminary injunction under subparagraph (B), the reference product sponsor and the subsection (k) applicant shall reasonably cooperate to expedite such further discovery as is needed in connection with the preliminary injunction motion.

(9) **LIMITATION ON DECLARATORY JUDGMENT ACTION**-

(A) **SUBSECTION (k) APPLICATION PROVIDED**- If a subsection (k) applicant provides the application and information required under paragraph (2)(A), neither the reference product sponsor nor the subsection (k) applicant may, prior to the date notice is received under paragraph (8)(A), bring any action under section 2201 of title 28, United States Code, for a declaration of infringement, validity, or enforceability of any patent that is described in clauses (i) and (ii) of paragraph (8)(B).

(B) **SUBSEQUENT FAILURE TO ACT BY SUBSECTION (k) APPLICANT**- If a subsection (k) applicant fails to complete an action required of the subsection (k) applicant under paragraph (3)(B)(ii), paragraph (5), paragraph (6)(C)(i), paragraph (7), or paragraph (8)(A), the reference product sponsor, but not the subsection (k) applicant, may bring an action under section 2201 of title 28, United States Code, for a declaration of infringement, validity, or enforceability of any patent included in the list described in paragraph (3)(A), including as provided under paragraph (7).

(C) **SUBSECTION (k) APPLICATION NOT PROVIDED**- If a subsection (k) applicant fails to provide the application and information required under paragraph (2)(A), the reference product sponsor, but not the subsection (k) applicant, may bring an action under section 2201 of title 28, United States Code, for a declaration of infringement, validity, or enforceability of any patent that claims the biological product or a use of the biological product.

(m) Pediatric Studies-

(1) **APPLICATION OF CERTAIN PROVISIONS**- The provisions of subsections (a), (d), (e), (f), (i), (j), (k), (l), (p), and (q) of section 505A of the Federal Food, Drug, and Cosmetic Act shall apply with respect to the extension of a period under paragraphs (2) and (3) to the same extent and in the same manner as such provisions apply with respect to the extension of a period under subsection (b) or (c) of section 505A of the Federal Food, Drug, and Cosmetic Act.

(2) **MARKET EXCLUSIVITY FOR NEW BIOLOGICAL PRODUCTS**- If, prior to approval of an application that is submitted under subsection (a), the Secretary determines that information relating to the use of a new biological product in the pediatric population may produce health benefits in that population, the Secretary makes a written request for pediatric studies (which shall include a timeframe for completing such studies), the applicant agrees to the request, such studies are completed using appropriate formulations for each age group for which the study is requested within any such timeframe, and the reports thereof are submitted and accepted in accordance with section 505A(d)(3) of the Federal Food, Drug, and Cosmetic Act--

(A) the periods for such biological product referred to in subsection (k)(7) are deemed to be 4 years and 6 months rather than 4 years and 12 years and 6 months rather than 12 years; and

(B) if the biological product is designated under section 526 for a rare disease or condition, the period for such biological product referred to in section 527(a) is deemed to be 7 years and 6 months rather than 7 years.

(3) **MARKET EXCLUSIVITY FOR ALREADY-MARKETED BIOLOGICAL PRODUCTS**- If the Secretary determines that information relating to the use of a licensed biological product in

the pediatric population may produce health benefits in that population and makes a written request to the holder of an approved application under subsection (a) for pediatric studies (which shall include a timeframe for completing such studies), the holder agrees to the request, such studies are completed using appropriate formulations for each age group for which the study is requested within any such timeframe, and the reports thereof are submitted and accepted in accordance with section 505A(d)(3) of the Federal Food, Drug, and Cosmetic Act--

(A) the periods for such biological product referred to in subsection (k)(7) are deemed to be 4 years and 6 months rather than 4 years and 12 years and 6 months rather than 12 years; and

(B) if the biological product is designated under section 526 for a rare disease or condition, the period for such biological product referred to in section 527(a) is deemed to be 7 years and 6 months rather than 7 years.

(4) **EXCEPTION**- The Secretary shall not extend a period referred to in paragraph (2)(A), (2)(B), (3)(A), or (3)(B) if the determination under section 505A(d)(3) is made later than 9 months prior to the expiration of such period.

(July 1, 1944, ch. 373, title III, Sec. 351, 58 Stat. 702; 1953 Reorg. Plan No. 1, Secs. 5, 8, eff. Apr. 11, 1953, 18 F.R. 2053, 67 Stat. 631; Pub. L. 85-881, Sec. 2, Sept. 2, 1958, 72 Stat. 1704; Pub. L. 91-515,title II, Sec. 291, Oct. 30, 1970, 84 Stat. 1308; Pub. L. 96-88, title V, Sec. 509(b), Oct. 17, 1979, 93 Stat. 695; Pub. L. 99-660, title I,Sec. 105(a), title III, Sec. 315, Nov. 14, 1986, 100 Stat. 3751, 3783; Pub. L. 102-300, Sec. 6(b)(1), June 16, 1992, 106 Stat. 240; Pub. L. 104-134, title II, Secs. 2102(d)(2), 2104, Apr. 26, 1996, 110 Stat. 1321-319, 1321-320; Pub. L. 105-115, title I, Sec. 123(a)-(d), (g), Nov. 21, 1997, 111 Stat. 2323, 2324; Pub. L. 111-148, March 23, 2010, sections (k)(l),(m))

This section is referred to in sections 236, 263, 300aa-22, 300aa- 23, 1396r-8 of this title; title 21 sections 321, 331, 352, 353, 355,356, 356a, 360aa, 360bb, 360cc, 360ee, 360aaa, 360bbb-1, 379g, 381, 382, 392, 397; title 26 section 45C; title 35 section 156.

EXHIBIT B

S/N 12/913,644 **PATENT**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Harry Cook et al.	Examiner: Unknown	
Serial No.:	12/913,644	Group Art Unit: 1614	
Filed:	October 27, 2010	Docket No.: 101.022US5	
Customer No.: 21186		Confirmation No.: 4280	
Title:	MICROBIOLOGICALLY SOUND AND STABLE SOLUTIONS OF GAMMA-HYDROXYBUTYRATE SALT FOR THE TREATMENT OF NARCOLEPSY		

PRELIMINARY AMENDMENT

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Prior to taking up this application for examination, please enter the following amendments:

Amendments to the Specification begin on page 2 of this paper;

Amendment to the Claims begin on page 32 of this paper; and

Remarks/Conclusion begin on page 34 of this paper.

IN THE SPECIFICATION

Please amend the specification as follows:

The paragraph beginning at page 4, line 17 is amended as follows:

The invention first provides a pharmaceutical composition of GHB rendered chemically stable and/or resistant to microbial growth in an aqueous medium. Preferred GHB salts of the present invention include sodium, ammonium and calcium. As used herein in certain embodiments, "stable" may mean resistant to degradation of GHB into its known or unknown decomposition elements. The level of GBL that is acceptable can be up to 0.1% of the formulation as per the ICH guidelines for shelf-life ~~determination,~~ determination. As used herein in certain embodiments, "resistant to microbial growth" or "resistant to microbial challenge" means that the formulations meet the criteria set by the Food and Drug Administration and the U.S. Pharmacopoeia for products made with aqueous bases or vehicles, which for bacteria means not less than a 1.0 log reduction from the initial count at 14 days, and no increase from the 14 days count at 28 days, and for yeast and molds, no increase from the initial calculated count at 14 and 28 days. As used herein in certain embodiments, an "aqueous medium" may mean a liquid comprising more than about 50% water. In certain preferred embodiments, an "aqueous medium" may be a solution, suspension, gel or emulsion of GHB, with a solution of GHB being most preferred. Preferred gels are thixotropic gels. Compositions that are resistant to microbial growth are created by dissolving or mixing GHB in an aqueous medium to a concentration or content of greater than of about 150 mg/ml GHB to the maximal solubility of GHB. The solubility of GHB is up to about 750 mg/ml at room temperature (20° C. to about 25° C.), however, heating the aqueous medium during preparation up to 100° C. will increase GHB solubility to at least about 1000 mg/ml. A preferred concentration or content of GHB is about 500 mg/ml.

The paragraph beginning at page 10, line 31 is amended as follows:

In certain embodiments, the pharmaceutical composition may contain a preservative. A "preservative" is understood herein to mean certain embodiments which are substances added to inhibit chemical change or microbial action. Such preservatives may include, but are not limited to, xylitol, sodium benzoate, methylparaben, propyl gallate BP, sorbic acid, chlorobutanol, dihydroacetic acid, monothioglycerol, potassium benzoate, propylparaben, benzoic acid, benzalkonium chloride, alcohol, benzoic acid, benzalkonium chloride, benzethonium chloride, benzyl alcohol, butylparaben, cetylpyridinium chloride, ethylenediamine, ~~ethylpareben,~~ ethylparaben, ethyl vanillin, glycerin, ~~hypophophorus~~ hypophosphorus acid, methylparaben, phenol, phenylethyl alcohol, ~~phenymercuric~~ phenylmercuric nitrate, propylparaben, sassafras oil, sodium benzoate, sodium propionate, thimerosal and potassium sorbate. Preferred preservatives may be selected from the group comprising, but not limited to, xylitol, sodium benzoate, methylparaben, propylparaben and potassium sorbate. Xylitol is particularly preferred in certain compositions of the invention, because it acts as an preservative and a sweetener, is a caries preventative, is less laxative than other sweeteners, and is recommended for diabetics.

The paragraph beginning at page 11, line 10 is amended as follows:

In certain embodiments, the pharmaceutical composition may also contain an antioxidant. An "antioxidant" is understood herein to mean certain embodiments which are substances that inhibits oxidation. Such antioxidants include, but are not limited to, ~~asocrbyl~~ ascorbyl palmitate, butylated hydroxyanisole, butylated hydroxytoluene, potassium metabisulfite, sodium metabisulfite, anoxomer and maleic acid BP.

The paragraph beginning at page 12, line 32 is amended as follows:

The invention also provides a method of treating any therapeutic category of disorder responsive to GHB, comprising administering to a patient suspected of having such a condition a therapeutic amount of a pharmaceutical composition comprising chemically stable GHB (e.g. 1-10 gms.) in an aqueous medium resistant to microbial growth. In certain embodiments, the method of treating a condition responsive to GHB comprises a patient taking a first dosage of from about 0.1 g to about 10 g, namely about 0.1, about ~~0.2~~ 0.2, about ~~0.3~~ 0.3, about 0.4, about 0.5, about 0.6, about 0.7, about 0.8, about 0.9, about 1.0, about 1.1, about 1.2, about 1.3, about 1.4, about 1.5, about 1.6, about 1.7, about 1.8, about 1-9, about 2.0, about 2.1, about 2.2, about 2.3, ~~about 2.3,~~ about 2.4, about 2.5, about 2.6, about 2.7, about 2.8, about 2.9, about 3.0, about 3.1, about 3.2, about 3.3, about 3.4, about 3.5, about 3.6, about 3.7, about 3.8, about 3.9, about 4.0, about 4.1, about 4.2, about 4.3, about 4.4, about 4.5, about 4.6, about 4.7, about 4.8, about 4.9, about 5.0, about 5.1, about 5.2, about 5.3, about 5.4, about 5.5, about 5.6, about 5.7, about 5.8, about 5.9, about 6.0, about 6.1, about 6.2, about 6.3, about 6.4, about 6.5, about 6.6, about 6.7, about 6.8, about 6.9, about 7.0, about 7.1, about 7.2, about 7.3, about 7.4, about 7.5, about 7.6, about 7.7, about 7.8, about 7.9, about 8.0, about 8.1, about 8.2, about 8.3, about 8.4, about 8.5, about 8.6, about 8.7, about 8.8, about 8.9, about 9.0 about 9.1, about 9.2, about 9.3, about 9.4, about 9.5, about 9.6, about 9.7, about 9.8, about 9.9, to about 10 grams of GHB, or as needed by the patient as would be recognized by one of skill in the art. Of course, it will be understood that all values in between those listed, such as 9.45 grams, 6.32 grams, etc. may be administered, and those values are encompassed well. In preferred embodiments, the first dose is administered within an hour of sleep. In preferred embodiments, a second dose of GHB within the values described above may be administered. This second dose is administered preferably within about 2.0 to about 5.0 hrs, namely about 2.0, about 2.1, about 2.2, about 2.3, ~~about 2.3,~~ about 2.4, about 2.5, about 2.6, about 2.7, about 2.8, about 2.9, about 3.0, about 3.1, about 3.2, about 3.3, about 3.4, about 3.5, about 3.6, about 3.7, about 3.8, about 3.9, about 4.0, about 4.1, about 4.2, about 4.3, about 4.4, about 4.5, about 4.6, about 4.7, about 4.8, about 4.9, to about 5.0 hours after the first dose, though it may be administered at a time outside of the preferred range.

The paragraph beginning at page 15, line 21 is amended as follows:

FIG. 1. The Range of Gamma-Hydroxybutyrate's Resistance to Microbial Growth and Chemical Stability in Aqueous Solution. The ordinate is the pH of solutions of GHB. The axis is the concentration (mg/ml) of GHB in aqueous solution. The region below the diagonal line [/] is the range of GHB solubility at room temperature. Greater solubility can be achieved, up to 1 g/ml, by heating the solution up to 100°C. ~~Three solutions were adjusted with HCl and were susceptible to microbial growth (Δ). Two solutions were pH adjusted with malic acid and were resistant to microbial growth (•). Of these two solutions, the one at pH 6 contained xylitol as an excipient. Three solutions were pH adjusted with hydrochloric acid and were resistant to microbial growth (>). One solution was not pH adjusted and was susceptible to microbial growth (*).~~

Table 2, beginning on page 16, is amended as follows:

TABLE 2

ID	Microbial Challenge Data Summary		
H	Sodium Oxybate Concentration	pH of Solution	Microbial Challenge Result
I	750 mg/cc	7.5 (HCl)	pass
J	500 mg/cc	6.0 (HCl)	pass
K	500 mg/cc + Excipients (Xylitol)	6.0 (Malic Acid)	pass
L	500 mg/cc	9.0 (HCl)	pass (borderline aspergillus)
M	150 mg/cc (BDL 1995)	5.0 (HCl)	fail (aspergillus only)
N	150 mg/cc (BDL 1995)	7.0 (HCl)	fail (aspergillus & staph)
O	150 mg/cc (BDL 1995)	3.0 (HCl)	fail (aspergillus only)
P	150 mg/cc (BDL 1995)	10.3 (unadjusted)	fail (aspergillus and staph)
Q	500 mg/cc	6.0 (Malic Acid)	discontinued
R	500 mg/cc	7.5 (Malic Acid)	pass

S	500 mg/cc (May '98)	9.0 (Malic Acid)	discontinued
T	500 mg/cc (May '98)	7.5 (HCl)	pass*
U	Others: 200 mg/cc-800 mg/cc	5.0-9.0	pending

*pass is generally defined as:

For Category 1C Products

Not less than 1.0 log reduction

Bacteria:

no from the initial ~~cout~~ count at 14 days, and increase from the 14 days' count at 28 days.

Yeast and Molds: No increase from the initial calculated count at 14 and 28 days.

The paragraph beginning at page 18, line 19 is amended as follows:

Any of the above formulations may be prepared and/or packaged as a powdered or dry form for mixing with an aqueous medium before oral administration, or they may be prepared in an aqueous medium and packaged. After mixing with an aqueous medium, ~~preferrably~~ preferably to prepare a solution, these formulations are resistant to both microbial growth and chemical conversion of GHB to GBL, thereby increasing the shelf-life of therapeutic formulations of GHB in an aqueous medium. These formulations-then provide an easily titratable liquid medium for measuring the dosage of GHB to be administered to a patient. Additional embodiments of the composition and methods of preparation are described below and in the examples.

The paragraph beginning at page 22, line 1 is amended as follows:

The ~~perferred~~ preferred oral formulations may include such normally employed excipients, as, for example, pharmaceutical grades of xylitol, mannitol, lactose, starch, magnesium stearate, sodium saccharin, cellulose, magnesium carbonate and the like. These compositions can take the form of solutions, suspensions, tablets, pills, capsules, sustained release formulations or powders to be admixed with an aqueous medium. In

certain defined embodiments, oral pharmaceutical compositions will comprise an inert diluent or assimilable edible carrier, or they may be enclosed in hard or soft shell gelatin capsule, or they may be compressed into tablets, or the GHB may be packaged separately from or in combination with the excipients, salts, flavorings or any other components described herein, to be admixed with an aqueous medium for oral or injectable formulations, or they may be incorporated directly with the food (i.e. a beverage) of the diet.

The paragraph beginning at page 22, line 22 is amended as follows:

The tablets, troches, pills, capsules and the like may also contain the following: a binder, ~~nutural~~ natural as gum tragacanth, acacia, cornstarch, or gelatin or synthetic as polyvinyl acetate; excipients, such as dicalcium phosphate; a disintegrating agent, such as corn starch, potato starch, alginic acid and the like; a lubricant, such as magnesium stearate; and a sweetening agent, such as sucrose, lactose or saccharin may be added or a natural or synthetic flavoring agent. When the dosage unit form is a capsule for admixing with a specific volume of an aqueous medium, it may contain, in addition to materials of the above type, a liquid carrier. Various other materials may be present as coatings or to otherwise modify the physical form of the dosage unit. For instance, tablets, pills, or capsules may be coated with sugar, natural or synthetic polymers, or both. A syrup or elixir may contain the active compounds, sucrose as a sweetening agent, a preservative, a dye and/or a flavoring.

The paragraph beginning at page 25, line 18 is amended as follows:

The inventors developed a liquid formulation composed of GHB, xylitol, and preservative in water (XYREM®). Subsequent instability of the preservative in this formulation and a desire to initiate clinical trials in a timely manner led to a change in the formulation to a foil pouch. One clinical trial utilized a twin-pouch dosage form, with one side (pouch 1) of the foil packet containing GHB and the other side (pouch 2) containing

the flavoring agents (Xylitol, [NF]; Malic Acid, ~~NF;~~ NF.

The paragraph beginning at page 27, line 6 is amended as follows:

The concentration and volume of the GHB solution that the patient administers will be the same irrespective of whether it is dissolved from the pouch or diluted from the liquid. This is illustrated in Chart 1 and Table 4:

Chart 1 Comparison of Liquid Solution to Twin-Pouch

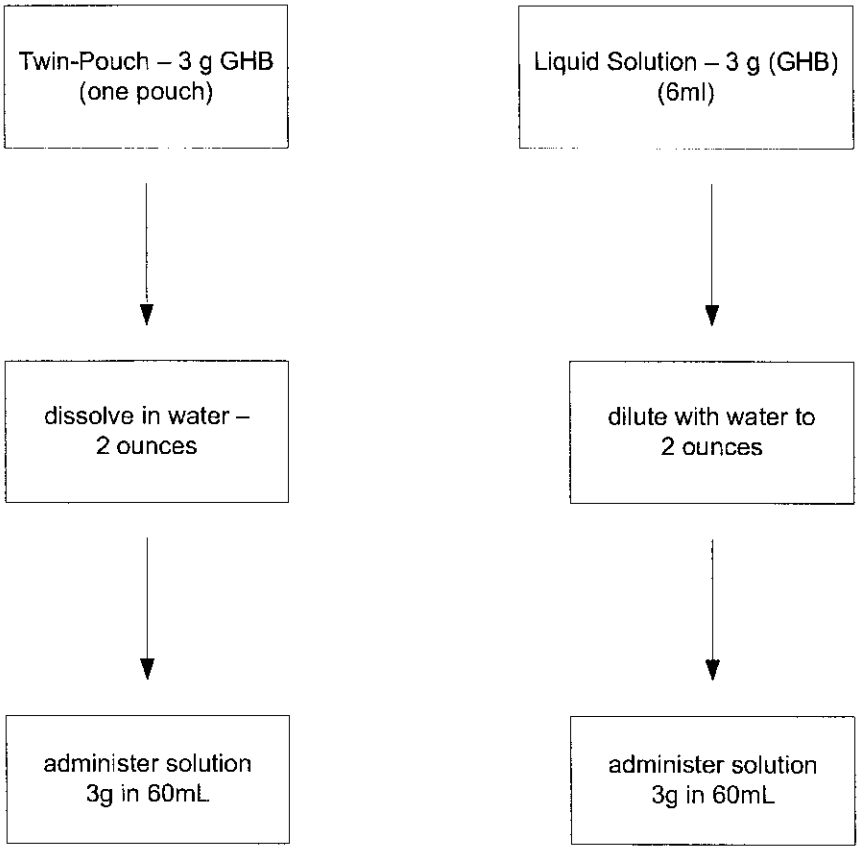

TABLE 4

Comparison of Liquid Solution to Twin-Pouch

	Twin-Pouch	Liquid Solution
Amount of GHB	3 grams (1 pouch)	3 grams (6 mL)
Inactive Components	malic acid Xylitol lemon/lime flavor Orange flavor	malic acid
Final Concentration	50 mg/mL	50 mg/mL*
Final Volume	60 mL	60 mL

*Final concentration outside the range of the most stable formulation. This formulation strength may be only stable at short periods of time such as 48 hours. The twin pouch version could be solubilized at a [[a]] concentration within the preferred range of pH and GHB concentration for longer term storage.

The paragraph beginning at page 27, line 6 is amended as follows:

Preservative effectiveness studies were conducted to identify a suitable preservative for the GHB liquid formulation. The following formulations shown in Table 5 were prepared and tested using *Staphylococcus ~~attreus~~ aureus* (ATCC #6538), *Pseudomonas aeruginosa* (ATCC #9027) and *Aspergillus niger* (ATCC #16404).

The paragraph beginning at page 31, line 1 is amended as follows:

The pH of all formulations migrated upward over the three month stability period ~~60C~~ at 60°C. The percent increase in pH from initial to 3 months, was greater for the formulations which were initially adjusted to lower values.

The paragraph beginning at page 31, line 4 is amended as follows:

For example, the migration of pH in formulations ~~1,3~~ 1, 3 and 4 (adjusted down to pH 3) were 21-30 percent across all conditions in three months. The migration of pH in formulations 2 and 5 (adjusted down to ~~pH5~~ pH 5) were 4.2-12 percent across all conditions in 3 months. Maintenance of pH becomes important for long term storage since preservatives are known to degrade in formulations having pH levels above approximately pH 6.

The paragraph beginning at page 31, line 10 is amended as follows:

Additionally, development of flavor systems to mask the negative taste of ~~perservatives~~ preservatives is difficult.

Table 17, on page 32, is amended as follows:

TABLE 7

Table 7

Results of Liquid Formulation Informal Stability Study at Three Months

Formulation # (See Table 6	Attribute	25° C./60% RH Upright	25° C./60% RH Inverted	40° C./75% RH Upright	40° C./75% RH Inverted	60° C. Upright
1	% t = 0	100.7	101.6	101.2	NA	NA
Potassium	pH	3.63	3.64	3.84	3.82	3.91
Sorbate (pH) at 3 months storage	Appearance	Clear, colorless	clear, colorless	clear, colorless	clear, colorless	clear, light yellow
2	% t = 0*	102.1	105.0	104.0	102.0	99.6
Potassium	pH	5.21	5.28	5.55	5.56	5.61
Sorbate (pH5)	Appearance	Clear, colorless	clear, colorless	clear, colorless	clear, colorless	clear, light brown
3	% t = 0	102.4	104.1	99.1	102.6	97.0
Sodium	pH	3.60	3.74	3.78	3.75	3.79
Benzoate (pH3)	Appearance	Clear, colorless	clear, colorless	clear, colorless	clear, colorless	clear, colorless
4	% t = 0	101.5	102.7	100.6	101.2	93.7
4 Methyl &	pH	3.63	3.71	3.81	3.80	3.83
Propyl ~~Parabense~~ Parabens (pH3)	Appearance	Clear, colorless	clear, colorless	clear, colorless	clear, colorless	clear, colorless
5	% t = 0	103.1	105.8	101.9	103.1	95.6
4 methyl &	pH	5.22	5.55	5.55	5.56	5.60
Propyl ~~Prabens~~ Parabens (pH5)	Appearance	Clear, colorless	clear, colorless	clear, colorless	clear, colorless	clear, light yellow

*% GHB at t = 0 percent of label claim

** initial time (t = 0)

The paragraph beginning at page 33, line 10 is amended as follows:

Developing a flavor system for the primary and back-up liquid formulations proved to be difficult and a decision was made to develop a dry powder formulation for reconstitution with water before consumption. This approach removed the need for a preservative system, the requirement to adjust pH to levels below ~~pH6~~ pH 6, and allowed the development of a suitable flavor system.

Table 10 on page 34, is amended as follows:

TABLE 10

Dry Powder Informal Stability Study Protocol

	Stability Time in Months						
Storage Conditions	0	1	2	3	6	9	12
40 ± 2° C./75% ± 5% RH		X	X	X	X		
25 ± 2° C./60% ± 5% RH	X	X	C	C	R	R	R

X = Samples to be tested
C = Contingency Samples
R = Reduced testing: assay and [[H_20]] H_2O only
RH = Relative Humidity

Table 12 on page 38, is amended as follows:

TABLE 12

Screening/Washout⇒	Treatment/Blood Sampling⇒	Follow-up
(1 or more days to dosing; washout, at least 8 h)	(Two 3 g GHB oral doses, 4 h apart; 21 blood samples)	(Within 48 h after last blood sample)

The paragraph beginning at page 43, line 18 is amended as follows:

Data Base: An EXCEL data base (spreadsheet) was constructed from data

recorded on Case Report Forms ~~(CFR)~~ (CRF) and plasma GHB concentration data sets received from Covance (Corning Hazleton). Each entry in the EXCEL spreadsheet was checked against the CRFs and any data entry error found was corrected.

The paragraph beginning at page 43, line 29 is amended as follows:

Pharmacokinetic Analysis: Pharmacokinetic parameters were determined for individual sets of plasma GHB concentration vs. time data using the non-compartmental routine in WinNonlin Version 1.1. The peak GHB concentrations (C_{max}) and the times of their respectively occurrences (t_{max}) were observed values. Terminal half-life ($T_{1/2}$) was obtained by log-linear regression analysis of the terminal phase of concentration vs. time curves. The area under the curve (AUC_{inf}) and the area under the first moment curve ($AUMC_{inf}$) were calculated by the linear trapezoidal rule up to the last determined concentration and included extrapolated areas to time infinity. Apparent oral clearance (CL/F) was calculated as Dose/AUC_{inf}. Volume of distribution ~~(Vz/F)~~ (V_z/F) was determined by taking the ratio between CL/F and λ_z (elimination rate constant). Mean residence time (MRT) was estimated from the ratio between $AUMC_{inf}$ and AUC_{inf}.

The paragraph beginning at page 44, line 11 is amended as follows:

All six patients took non-study medications in addition to methylphenidate and GHB doses because none of their concomitant medications (~~Synthyroid,~~ Synthroid, Premarin, Lovastatin, ~~Flovastatin,~~ Fluvastatin, furosemide, potassium, hydrochlorothiazide, lansoprazole, and verapamil) were on the exclusion list (which included hypnotics, sedatives, antidepressants, antihistamines, clonidine, and anticonvulsants). Adverse experience probes, vital sign measurements, and essentially all pharmacokinetic blood samples were performed at protocol specified times; the few deviations in blood sampling times should not have any impact on the outcome of the study since actual blood sampling times were used in the pharmacokinetic analysis.

The paragraph beginning at page 48, line 10 is amended as follows:

a. Rapid Mix Method:

The paragraph beginning at page 48, line 13 is amended as follows:

Sodium oxybate was dissolved in water and concentrated acidulent was added immediately, without temperature control. Temperature of solution was monitored and recorded prior to and during addition of acidulent. The time of ~~equiliberation~~ equilibration to room temperature was also recorded. After the solution reached ambient room temperature, it was filtered through a 10 μm filter.

The paragraph beginning at page 48, line 28 is amended as follows:

d. Sodium Oxybate Control:

The paragraph beginning at page 49, line 8 is amended as follows:

The following methods were used to test the prepared solutions: pH, HPLC (High Pressure Liquid ~~Chromotography~~ Chromatography) for potency (sodium oxybate), and for impurities. Time 0 analysis was performed immediately (within 24 h). RRT=(relative retention time).

The paragraph beginning at page 54, line 24 is amended as follows:

Microbial challenge testing of formulations was preformed according to USP XXIII, <51>, Eighth Supplement. Solutions are determined to "Pass or Fail" based upon the USP criteria for ~~perservative~~ preservative effectiveness which states: For Bacteria, "Not less than 1 log reduction from the initial microbial count at 14 days and no increase from the 14 days count at 28 days;" and for yeast and molds, "No increase from the initial

calculated count at 14 and 28 days." Solutions which met these criteria were designated as "Pass" and those that did not meet these criteria were designated as "Fail".

The paragraph beginning at page 55, line 21 is amended as follows:

HCl, pH 7.5 formulation (25%) GBL levels measured ~~0.041%~~ 0.041% on Day 0, Impurity A measured 0.02%, and by Day 18 GBL measured to 0.12% and impurity A to 0.07%. Under accelerated conditions (40° C. and 60° C.), GBL increased to a maximum of 0.21%, impurity A increased from 0.02% to 0.1%, and pH increased from 7.5 to 8.0. As with Malic Acid at pH 7.5, the measured parameters reached maximum by Day 7 and did not increase significantly thereafter.

Table 17 on page 59, is amended as follows:

TABLE 17

Formulation Detail				
Formulation ID No.	Salt of GHB	Concentration of Salt of GHB	~~Acidultent~~ Acidulent	Final pH
9	Calcium salt	500 mg/cc (Or maximum possible*)	Malic Acid (If compatible)	7.5

Table 19, beginning on page 64, is amended as follows:

Table 19

Result Summary
Data from Dec. 30, 1997

	(n = 3) Inoculu	0	Day 1	Day 3	Day 7	Day 14	Day 21	Day 28	Results
GHB (pH 7.5) 750 mg/cc									
E. coli	470,000	160,000	64,500	4,300	420	<10	<10	<10	
~~*P. aeruginos*~~ *P. aeruginosa*	437,500	152,000	3,500	10	<10	<10	<10	<10	
S. aureus	447,500	330,000	24,500	42,000	8,050	1,935	15	10	
C. albicans	375,000	234,500	28,000	1,950	<10	<10	10	<10	
A. niger	475,500	395,000	395,000	229,000	101,500	161,500	101,000	202,000	
750 mg/cc + 0.20% MP/PP pH 7.50									
E. coli	470,000	127,000	<1,000	<10	<10	<10	<10	<10	
~~*P. aeruginos*~~ *P. aeruginosa*	437,500	61,000	<1,000	<10	<10	<10	<10	<10	
S. aureus	447,500	350,000	3,000	4,050	<10	<10	<10	<10	
C. albicans	375,000	103,500	<1,000	<10	<10	<10	<10	<10	
A. niger	457,500	315,000	415,000	35,500	79,500	38,500	87,500	6,400	
750 mg/cc + 0.1% MP/PP, pH 7.5									
E. coli	470,000	157,000	7,000	<10	<10	<10	<10	<10	

Result Summary
Data from Dec. 30, 1997

	(n = 3) Inoculu	0	Day 1	Day 3	Day 7	Day 14	Day 21	Day 28	Results
~~*P. aeruginos*~~ *P. aeruginosa*	437,500	90,000	<1,000	<10	<10	<10	<10	<10	
S. aureus	447,500	239,000	5,500	16,950	600	<10	<10	<10	
C. albicans	375,000	169,000	<1,000	<100	<10	<10	<10	<10	
A. niger	457,500	335,000	425,000	34,500	168,500	90,500	95,500	99,000	
750 mg/cc + 0.2% Potassium sorbate, pH 7.5									
E. coli	470,000	180,000	735,000	6,200	475	<10	<10	<10	
~~*P. aeruginos*~~ *P. aeruginosa*	437,500	152,000	1,000	<10	<10	<10	<10	<10	
S. aureus	447,500	264,000	27,500	49,800	14,550	2,370	<10	<10	
C. albicans	375,000	300,000	41,500	3,800	<10	<10	<10	<100	
A. niger	457,500	325,000	360,000	25,000	202,000	500,000	345,000	425,000	
GHB (pH 6.0) 500 mg/cc									
E. coli	470,000	221,000	40,000	100	<10	<10	<10	<10	
P. aeruginosa	437,500	172,000	3,000	<10	<10	<10	<10	<10	
S. aureus	447,500	320,000	<1,000	30	<10	<10	<10	<10	
C. albicans	375,000	310,000	14,000	100	<10	<10	<10	<10	
A. niger	475,500	270,000	355,000	84,000	120,000	48,500	41,000	8,600	
500 mg/cc + 0.2%									PASS

Result Summary
Data from Dec. 30, 1997

	(n = 3) Inoculu	0	Day 1	Day 3	Day 7	Day 14	Day 21	Day 28	Results
MP/PP, pH 6.0									
E. coli	470,000	163,000	<1,000	<10	<10	<10	<10	<10	
P. aeruginosa	437,500	60,000	<1,000	<10	<10	<10	<10	<10	
S. aureus	447,500	243,000	<1,000	<10	<10	<10	<10	<10	
C. albicans	375,000	150,500	<1,000	<100	<10	<10	<10	<10	
A. niger	475,500	400,000	38,000	<10	<10	<10	<10	<10	
									PASS
500 mg/cc + 0.1% MP/PP, pH 6.0									
E. coli	470,000	206,000	<1,000	<10	<10	<10	<10	<10	
P. aeruginosa	437,500	118,000	<1,000	<10	<10	<10	<10	<10	
S. aureus	447,500	330,000	<1,000	<10	<10	<10	<10	<10	
C. albicans	375,000	221,000	<1,000	<100	<10	<10	<10	<10	
A. niger	475,500	355,000	93,500	59,000	8,700	315	35	<10	
									PASS
500 mg/cc + 0.2% Potassium sorbate, pH 6.0									
E. coli	470,000	222,000	46,500	150	<10	<10	<10	<10	
P. aeruginosa	437,500	136,000	<1,000	<10	<10	<10	<10	<10	
S. aureus	447,500	410,000	<1,000	130	<10	<10	<10	<10	

Result Summary
Data from Dec. 30, 1997

	(n = 3) Inoculu	0	Day 1	Day 3	Day 7	Day 14	Day 21	Day 28	Results
C. albicans	375,000	395,000	28,500	<100	<10	<10	<10	<10	
A. niger	475,500	405,000	270,000	63,000	51,000	49,500	39,000	11,150	
									PASS

Table 21, beginning on page 68, is amended as follows:

TABLE 21

Result Summary

GHB (pH 7.50)	HCl	Jul. 2, 1998 Start Date						
500 mg/cc	Initial Conc	0	Day 1	Day 3	Day 7	Day 14	Day 21	Day 28
E. coli	97000	82000	19200	nd	1000	<10	<10	<10
P. aeruginosa	48500	29500	520	nd	<10	<10	<10	<10
S. aureus	54500	58000	42350	nd	4950	245	<10	<10
C. albicans	58500	38500	1060	nd	<100	<10	<10	<10
A. niger	77500	48000	21450	nd	46000	46000	38000	54000
GHB (pH 7.50)	Malic Acid							
500 mg/cc	Initial Conc	0	Day 1	Day 3	Day 7	Day 14	Day 21	Day 28
E. coli	97000	83000	44450	nd	3050	70	<10	<10
P. aeruginosa	48500	15650	545	nd	<10	<10	<10	<10
S. aureus	54500	59500	48400	nd	17400	6500	820	505
C. albicans	58500	44000	6200	nd	500	<10	<10	<10
A. niger	77500	35500	24100	nd	28000	49000	44500	44000

Result Summary

GHB (pH 7.50)	HCl	Jul. 2, 1998 Start Date						
500 mg/cc	Initial Co	0	Day 1	Day 3	Day 7	Day 14	Day 21	Day 28
E. coli	9.70E+04	8.20E+04	1.92E+04	nd	1.00E+03	<10	<10	<10
P. aeruginosa	4.85E+04	2.95E+04	5.20E+02	nd	<10	<10	<10	<10
S. aureus	5.45E+04	5.80E+04	4.24E+04	nd	4.95E+03	2.45E+02	<10	<10
C. albicans	5.85E+04	3.85E+04	1.06E+03	nd	<100	<10	<10	<10
A. niger	7.75E+04	4.80E+04	2.15E+04	nd	4.60E+04	4.60E+04	3.80E+04	5.40E+04
GHB (pH 7.50)	Malic Acid							
500 mg/cc	Initial Co	0	Day 1	Day 3	Day 7	Day 14	Day 21	Day 28
E. coli	9.70E+04	8.30E+04	4.45E+04	nd	3.05E+03	7.00E+01	<10	<10
P. aeruginosa	4.85E+04	1.57E+04	5.45E+02	nd	<10	<10	<10	<10
S. aureus	5.45E+04	5.95E+04	4.84E+04	nd	1.74E+04	6.50E+03	8.20E+02	5.05E+02
C. albicans	5.85E+04	4.40E+04	6.20E+03	nd	5.00E+02	<10	<10	<10
A. niger	7.75E+04	3.55E+04	2.41E+04	nd	2.80E+04	4.90E+04	4.45E+04	4.40E+04

For Category IC Products:

Bacteria: Not less ~~that~~ than 1 log reduction from the initial count at 14 days, and no increase from the 14 days count at 28 days.

Yeast and Molds: No increase from the initial calculated count at 14 and 28 days.

The paragraph beginning at page 72, line 3 is amended as follows:

Short term stability testing was carried out as described in Appendix A and results are summarized in--Results of Limited Stability Testing--~~Xyrem~~ XYREM® oral solution-- are show as follows:

Table 23-F, on page 77, is amended as follows:

TABLE 23-F

ORPHAN MEDICAL INC.
13911, Ridgedale Drive
Minnetonka, (MN) 55305
USA

DATE: 21/01/1999
NO.: 331345

CERTIFICATE OF ANALYSIS

OXYBATE SODIUM, LIQUID FORMULATION
PROTOCOL 98126
ORPHAN MEDICAL

LOT: MCH1064-3
CODE:
REQUISITION: 1741

TEST	SPECIFICATION	~~RESULTAT/RESULT~~ RESULT	PROCEDURE
Description	Clear to slightly opalescent solution.	Conforms	ORGANOLEPTIC
Potency	Report	363 mg/ml (104%)	NPLC-793-D
Impurities total	≤2.0%	0.21%	NPLC-793D
Impurities specified	Gamma-Butyrolactone (RRT = 1.6): ≤0.5%	RRT 1.46: 0.14%	NPLC-793D
	Impurity A (RRT 4.3): ≤0.5%	RRT 4.31: 0.05%	
Impurities unspecified	Ind. imp. ≤0.1%	*A	NPLC-793D
PH	Report	8.0	USP <791>

COMMENTS:
28 DAYS (25° C., 60% RH)
Formulation 3: 350 mg/cc; Malic acid; pH 7.5

*A: RRT 1.29: 0.009% RRT 3.93: 0.008%

The paragraph beginning at page 86, Table 23-O is amended as follows:

TABLE 23-O

ORPHAN MEDICAL INC.
13911, Ridgedale Drive
Minnetonka, (MN) 55305
USA

DATE: 09/02/1999
NO.: 330721

CERTIFICATE OF ANALYSIS

OXYBATE CALCIUM LIQUID FORM.
(28 DAYS CHALLENGE TEST)
PROTOCOL 98126
ORPHAN MEDICAL

LOT: MCH1064-85
CODE:
REQUISITION: 1741

TEST	SPECIFICATION	RESULT	PROCEDURE
Description	Clear to slightly opalescent solution	Conforms	ORGANOLEPTIC
Challenge Test	Conforms to USP (0, 1, 7, 14, 21 and 28)	Conforms	USP 23 <51>5.8
Potency	Report	501 mg/ml (100%)	NPLC-793
Impurities total	≤2.0%	1.2%	NPLC-793D
Impurities unspecified	Ind. imp. ≤0.1%	*A	NPLC-793D
Impurities specified	Gamma-Butyrolactone Report:	RRT 1.46: 0.013%	NPLC-793D
PH	Report	7.3	USP <791>
Solubility study	Report	*B	PR 98126 IIA

COMMENTS:
Initial test
500 ~~mg/ml cc~~ mg/cc; Malic acid; pH 7.5
*A: RRT 1.31: 0.02% RRT 1.67: 0.008%
RRT 1.91: Interference with peak of dilution solvent cannot calculate.
RRT 3.47: 0.1% RRT 3.79: 0.009% RRT 3.84: 0.01%
RRT 4.18: 0.06% RRT 5.10: 0.008% RRT 5.35: 0.02%
RRT 6.74: 0.9% RRT 6.90: 0.08% RRT 7.41: 0.006%
*B: Maximum solubility: 700 mg/ml no pH adjustment.

Table 24, on page 89, is amended as follows:

TABLE 24
Testing of Sodium and Calcium GHB Salts

	pH of Solutions	Microbial Challenge Result
Sodium Oxybate Concentration		
1. 500 mg/cc	7.5 (Malic acid)	Pass
2. 250 mg/cc	7.5 (Malic acid)	Pass
3. 350 mg/cc	7.5 (Malic acid)	Pass
4. 450 mg/cc	7.5 (Malic acid)	Pass
5. 550 mg/cc	7.5 (Malic acid)	Pass
6. 650 mg/cc	7.5 (Malic acid)	Pass
7. 500 mg/cc	7.5 (Citric acid)	Pass
Calcium Oxybate ~~Conctration~~ Concentration		
500 mg/cc	7.5	Pass

Table 25, beginning on page 90, is amended as follows:

TABLE 25
Sodium and Calcium GHB Evaluation

Sodium oxybate solution	Potency mg/cc (%)	Impurities (Total)	Impurities (Unspecified)	Impurities (Specified – ~~GLB~~ GBL)	pH
500 mg/cc pH 7.5 Malic Acid Day 0	512 mg/cc (102%)	0.68%	0.041%	0.027%	7.6
Day 28	510 mg/cc (103%)	0.36%	0.33%	0.028%	7.9
250 mg/cc pH 7.5 Malic Acid Day 0	258 mg/cc (103%)	0.045%	0.009%	0.026%	7.6

Day 28	256 mg/cc (102%)	0.18%	0.015%	0.16%	7.9
350 mg/cc pH 7.5 Malic Acid Day 0	360 mg/cc (103%)	0.050%	0.013%	0.037%	7.7
Day 28	363 mg/cc (104%)	0.21%	0.017%	0.19%	8.0
450 mg/cc pH 7.5 Malic Acid Day 0	461 mg/cc (102%)	0.065%	0.027%	0.038%	7.5
Day 28	454 mg/cc (101%)	0.40%	0.038%	0.36%	7.8
550 mg/cc pH 7.5 Malic Acid Day 0	563 mg/cc (102%)	0.077%	0.037%	0.040%	7.6
Day 28	561 mg/cc (102%)	0.56%	0.047%	0.51%	7.9
650 mg/cc pH 7.5 Malic Acid Day 0	666 mg/cc (102%)	0.10%	0.057%	0.045%	7.6
Day 28	660 mg/cc (102%)	0.81%	0.077%	0.73%	7.8
500 mg/cc pH 7.5 Malic Acid Day 0	518 mg/cc (104%)	0.065%	0.027%	0.038%	7.5
Day 28	515 mg/cc (103%)	0.38%	0.007%	0.37%	7.9

Calcium oxybate solution	Potency	Impurities (Total)	Impurities (Specified)	Impurities (Unspecified)	pH
500 mg/cc pH 7.5 Malic Acid	501 mg/cc (100%)	1.2%	>0.1% (See C of A Attached)	0.013%	7.3

Day 0 Day 28	508 mg/cc (102%)	0.70%	>0.1% (See C of A)	0.054%	7.6

The paragraph beginning at page 94, line 19 is amended as follows:

Arena and Fung, "Absorption of sodium γ-hydroxybutyrate and its prodrug γ-butyrolactone: relationship between ~~n vitro~~ in vitro transport and in vivo absorption," *J. Pharmaceutical Sciences*, 69(3):356-358, 1980.

The paragraph beginning at page 94, line 30 is amended as follows:

Broughton and Mamelak, "The treatment of narcolepsy-cataplexy with ~~noctural~~ nocturnal gamma-hydroxybutyrate," *Le Journal Canadien Des Sciences Neurologiques*, 6(1):1-6, 1979.

The paragraph beginning at page 94, line 30 is amended as follows:

Ferrara, Zotti, Tedeschi, Frison, Castagna, Gallimberti, Gessa, "Pharmacokinetics of ~~γ-hydroxybutyric~~ γ-hydroxybutyric acid in alcohol dependent patients after single and repeated oral doses," *Br. J. Clin. Pharmacol.*, 34:231-235, 1992.

The paragraph beginning at page 95, line 14 is amended as follows:

Gallimberti et al., "Gamma-~~Hydroxybutrie~~Hydroxybutyric Acid in the Treatment of Alcohol Dependence: A Double-Blind Study" *Clin. Exp. Res.*, 16, 673-676, 1992.

The paragraph beginning at page 95, line 20 is amended as follows:

Gessa, Diana, Fadda, Colombo, "Gamma-hydroxybutyric acid ~~(GHHHB)~~ (GHB) for treatment of ethanol dependence," *Clin. Neuropharm.-Supplement*, 1992.

The paragraph beginning at page 96, line 18 is amended as follows:

~~Lammers, Arends, Declerck, Ferrari, Schouwink, Troost, "Gammahydroxybutyrate and Narcolepsy: A Double-Blind Placebo-Controlled Study," Sleep, 16(3):216-220, 1993.~~

The paragraph beginning at page 97, line 1 is amended as follow:

~~Lee, "Evidence for the .beta.-Oxidation of Orally Administered 4-Hydroxybutyrate in Humans," Biochemical Medicine, 17, 284-291, 1977.~~

The paragraph beginning at page 98, line 1 is amended as follows:

~~Nema et al., "Excipients and their use in injectable products," PDA J Pharm Sci Technol., 51(4):166-171,1997.~~

The paragraph beginning at page 98, line 26 is amended as follows:

~~Scrima, Hartman, Johnson, Thomas, Hiller, "The effects of gamma-hydroxybutyrate on the sleep of narcolepsy patients: A double blind study," Sleep Res., 13:479-490, 1990.~~

The paragraph beginning at page 100, line 3 is amended as follows:

~~Vickers, Int. Anesth. Clinic 7:75-89, 1969;~~

IN THE CLAIMS

Please amend the claims as follows:

Claims 1-22 (Canceled).

23. (New) A method of treating a condition responsive to sodium gamma-hydroxybutyrate, comprising
(i) diluting an aqueous solution comprising about 500 mg/mL of sodium gamma-hydroxybutyrate with an aqueous medium to provide a first dose of about 4.5 to about 10 grams of sodium gamma-hydroxybutyrate;
(ii) diluting an aqueous solution comprising about 500 mg/mL of sodium gamma-hydroxybutyrate with an aqueous medium to provide a second dose of about 4.5 to about 10 grams of sodium gamma-hydroxybutyrate;
(iii) orally administering to a patient afflicted with the condition the first dose within an hour prior to initial sleep onset;
(iv) orally administering to a patient afflicted with the condition the second dose within 2.5 to 4 hours following initial sleep onset;
wherein the condition is cataplexy or daytime sleepiness in a patient with narcolepsy.

24. (New) The method of claim 23, wherein each dose is about 4.5 grams of sodium gamma-hydroxybutyrate.

25. (New) The method of claim 24 in which each dose of about 4.5 grams of sodium gamma-hydroxybutyrate is prepared by diluting an aqueous solution comprising about 500 mg/mL of sodium gamma-hydroxybutyrate with about 60 mL of water.

26 (New) The method of any one of claims 23-25, wherein the first dose is orally administered to the patient immediately prior to bedtime.

27. (New) A method of treating a condition responsive to sodium gamma-hydroxybutyrate, comprising

(i) diluting an aqueous solution comprising about 500 mg/mL of sodium gamma-hydroxybutyrate with an aqueous medium to provide a first dose of about 3 to about 10 grams of sodium gamma-hydroxybutyrate;

(ii) diluting an aqueous solution comprising about 500 mg/mL of sodium gamma-hydroxybutyrate with an aqueous medium to provide a second dose of about 3 to about 10 grams of sodium gamma-hydroxybutyrate;

(iii) orally administering to a patient afflicted with the condition the first dose within an hour prior to initial sleep onset;

(iv) orally administering to a patient afflicted with the condition the second dose within 2.5 to 4 hours following initial sleep onset;

wherein the condition is cataplexy or daytime sleepiness in a patient with narcolepsy.

28. (New) The method of claim 27, wherein each diluted dose contains about 50 mg/mL to about 167 mg/mL sodium gamma-hydroxybutyrate.

29. (New) The method of claim 27, wherein each dose is about 3 to about 4.5 grams of sodium gamma-hydroxybutyrate.

30. (New) The method of claims 29, wherein each diluted dose contains about 50 mg/mL to about 75 mg/mL sodium gamma-hydroxybutyrate.

31. (New) The method of any one of claims 27-30, wherein the first dose is orally administered to the patient immediately prior to bedtime.

CONCLUSION

Claims 1-22 have been canceled. Claims 23-31 have been added. Applicant respectfully submits that no new matter was added. Thus, claims 23-31 are pending. Applicants respectfully submit that the claims (23-31) are in condition for allowance and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicants' representative at (612) 373-6905 to facilitate prosecution of this application.

If necessary, please charge any additional fees or deficiencies, or credit any overpayments to Deposit Account No. 19-0743.

Respectfully Submitted,

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Date January 10, 2010 By /Monique M. Perdok Shonka/
Monique M. Perdok Shonka
Reg. No. 42,989

Electronic Patent Application Fee Transmittal

Application Number:	12913644
Filing Date:	27-Oct-2010
Title of Invention:	MICROBIOLOGICALLY SOUND AND STABLE SOLUTIONS OF GAMMA-HYDROXYBUTYRATE SALT FOR THE TREATMENT OF NARCOLEPSY
First Named Inventor/Applicant Name:	Harry Cook
Filer:	Gregory M. Stark/John Gustav-Wrathall
Attorney Docket Number:	101.022US5

Filed as Small Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Multiple dependent claims	2203	1	195	195
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
			Total in USD ($)	**195**

Electronic Acknowledgement Receipt	
EFS ID:	9202837
Application Number:	12913644
International Application Number:	
Confirmation Number:	4280
Title of Invention:	MICROBIOLOGICALLY SOUND AND STABLE SOLUTIONS OF GAMMA-HYDROXYBUTYRATE SALT FOR THE TREATMENT OF NARCOLEPSY
First Named Inventor/Applicant Name:	Harry Cook
Customer Number:	21186
Filer:	Gregory M. Stark/John Gustav-Wrathall
Filer Authorized By:	Gregory M. Stark
Attorney Docket Number:	101.022US5
Receipt Date:	10-JAN-2011
Filing Date:	27-OCT-2010
Time Stamp:	19:21:10
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	$195
RAM confirmation Number	5806
Deposit Account	190743
Authorized User	
The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows: Charge any Additional Fees required under 37 C.F.R. Section 1.16 (National application filing, search, and examination fees) Charge any Additional Fees required under 37 C.F.R. Section 1.17 (Patent application and reexamination processing fees)	

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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		101022us5_pamd_011011.pdf	240274 3f4d4ee671c131e9348c53d86e74a244be72d517	yes	34

Multipart Description/PDF files in .zip description

Document Description	Start	End
Miscellaneous Incoming Letter	1	1
Preliminary Amendment	2	2
Specification	3	31
Claims	32	33
Applicant Arguments/Remarks Made in an Amendment	34	34

Warnings:

Information:

2	Fee Worksheet (PTO-875)	fee-info.pdf	30555 d701c2f763255d429095110db2f868bbd6539d58	no	2

Warnings:

Information:

Total Files Size (in bytes):	270829

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Harry Cook et al.

Title: MICROBIOLOGICALLY SOUND AND STABLE SOLUTIONS OF GAMMA-HYDROXYBUTYRATE SALT FOR THE TREATMENT OF NARCOLEPSY

Docket No.:	101.022US5	Serial No.:	12/913,644
Filed:	October 27, 2010	Due Date:	N/A
Examiner:	Unknown	Group Art Unit:	1614
Customer No.:	21186	Confirmation No.:	4280

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

We are transmitting herewith the following attached items (as indicated with an "X"):

X Preliminary Amendment (33 pgs.)
X Authorization to charge Deposit Account 19-0743 in the amount of $195.00 to cover the fee for additional claims.

The fee for additional claims has been calculated as follows:

CLAIMS AS AMENDED						
	Claims Remaining After Amendment		Highest Number Previously Paid For	Present Extra	Rate	Fee
TOTAL CLAIMS	0	-	20	0	x 26.00 =	0.00
INDEPENDENT CLAIMS	0	-	3	0	x 110.00 =	0.00
[X] MULTIPLE DEPENDENT CLAIMS PRESENTED						195.00
TOTAL						195.00

If not provided for in a separate paper filed herewith, please consider this a PETITION FOR EXTENSION OF TIME for sufficient number of months to enter these papers and please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

SCHWEGMAN, LUNDBERG & WOESSNER, P.A.
Customer No.: 21186

By: /Monique M. Perdok Shonka/
Monique M. Perdok Shonka
Reg. No. 42,989

PTO/SB/06 (07-06)
Approved for use through 1/31/2007. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

PATENT APPLICATION FEE DETERMINATION RECORD
Substitute for Form PTO-875

Application or Docket Number	Filing Date	☐ To be Mailed
12/913,644	10/27/2010	

APPLICATION AS FILED – PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	SMALL ENTITY ☒ RATE ($)	SMALL ENTITY ☒ FEE ($)	OR	OTHER THAN SMALL ENTITY RATE ($)	OTHER THAN SMALL ENTITY FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A			N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A			N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A			N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X $ =		OR	X $ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X $ =			X $ =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $250 ($125 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).						
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))							
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL			TOTAL	

APPLICATION AS AMENDED – PART II

AMENDMENT 01/10/2011	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	SMALL ENTITY RATE ($)	SMALL ENTITY ADDITIONAL FEE ($)	OR	OTHER THAN SMALL ENTITY RATE ($)	OTHER THAN SMALL ENTITY ADDITIONAL FEE ($)
Total (37 CFR 1.16(i))	* 9	Minus	** 22	= 0	X $26 =	0	OR	X $ =	
Independent (37 CFR 1.16(h))	* 2	Minus	***3	= 0	X $110 =	0	OR	X $ =	
☐ Application Size Fee (37 CFR 1.16(s))									
☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
					TOTAL ADD'L FEE	0	OR	TOTAL ADD'L FEE	

AMENDMENT	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)	OR	RATE ($)	ADDITIONAL FEE ($)
Total (37 CFR 1.16(i))	*	Minus	**	=	X $ =		OR	X $ =	
Independent (37 CFR 1.16(h))	*	Minus	***	=	X $ =		OR	X $ =	
☐ Application Size Fee (37 CFR 1.16(s))									
☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
					TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".
The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

Legal Instrument Examiner:
/SHARAIN MORELAND/

EXHIBIT C

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April 29, 2011

BY E-MAIL

Gabriel P. Brier
Jones Day
222 East 41st Street
New York, NY 10017-6702

Re: *Jazz Pharmaceuticals, Inc. v. Roxane Laboratories, Inc.*, Civil Action No. 10-6108 (SDW)(MCA) (D.N.J.)

Dear Gabe:

This responds to your correspondence dated April 28, 2011 regarding the proposed Scheduling Order.

We disagree that Roxane's proposal to exchange two rounds of expert reports, not three, is *not* a sensible approach. Our proposal does not require Plaintiff to submit expert reports in rebuttal to Roxane's expert(s)' opinions of obviousness of the claims of the patents-in-suit over the prior art. It merely proposes that Plaintiff submit any expert report(s) on the issue of secondary considerations of nonobviousness, namely commercial success, long felt but unsolved needs, failure of others, etc., *see Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966), during the first round of expert reports and does not suggest that Plaintiff submit its reports on the state of the prior art until the second round of expert reports. The factors of secondary considerations of nonobviousness set forth in *Graham v. John Deere* are not related to or dependent on the state of the prior art, which would be the subject of Roxane's invalidity expert report(s) submitted during the first round. For example, Plaintiff is required to prove the existence of commercial success (that the product is successful) and then prove that there is a nexus between the alleged commercial success of the product and the scope of the claims of the patents-in-suit. Roxane is at a loss as to how this type of showing cannot be made without first seeing Roxane's invalidity expert report(s). Moreover, by the time of the expert reports our invalidity contentions and state of the prior art will be evident to you.

As to your statement about the November 20, 2011 amended scheduling order from Civil Action No. 07-3770, while the order contemplated a third round, no third round was ever granted by Judge Cavanaugh.

Moreover, we disagree that "Roxane is now attempting to undo previous points of agreement." As evident in my emails to you dated April 11, 2011 and April 21, 2011 which are attached hereto, Roxane never agreed to three rounds of expert reports—Roxane merely requested further information to properly evaluate Plaintiff's proposal for three rounds—and based on Plaintiff's explanation and Roxane's understanding of that explanation, sought further

clarification as to when Plaintiff would submit its report(s) on secondary considerations of nonobviousness. Your email of April 25, 2011 flatly rejected our proposal. There never was any meeting of the minds as to what experts reports were to be exchanged in how many rounds.

In the spirit of compromise, however, Roxane would agree to Plaintiff's proposal to have three rounds of expert reports, if Plaintiff agrees to include the dates Roxane proposes for the pretrial conference (October 22, 2012 or any other date as is convenient for the Court) and for trial (December 10, 2012 or any other date as is convenient for the Court).

Please let us know whether Plaintiff agrees to Roxane's compromise.

Sincerely,

Miki Goodin

Attachments

cc: All counsel of record

EXHIBIT D

UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

ELI LILLY AND COMPANY, Plaintiff, v. ACTAVIS ELIZABETH LLC, GLENMARK PHARMACEUTICALS INC., USA, SUN PHARMACEUTICAL INDUSTRIES LIMITED, SANDOZ INC., MYLAN PHARMACEUTICALS INC., APOTEX INC., AUROBINDO PHARMA LTD.,TEVA PHARMACEUTICALS USA, INC., SYNTHON LABORATORIES, INC., ZYDUS PHARMACEUTICALS, USA, INC. Defendants.	)	Civil Action No. 07-3770 (DMC) (MF)

AMENDMENT TO PRETRIAL SCHEDULING ORDER

This matter having come before the Court upon the parties' stipulation and consent to amend certain discovery deadlines, and the Court having been fully advised that the parties require these adjustments to complete and facilitate discovery relating to the substantive issues of this litigation; and the Court having considered the pleadings in this matter, and for other and good cause appearing:

IT IS HEREBY ORDERED on this 20 day of November, 2008, that the Pretrial Scheduling Orders dated December 18, 2007 (Docket No. 109) and July 17, 2008 (Docket No. 192) are modified as follows:

1. Date for delivery of affirmative expert reports including secondary considerations by Plaintiff: December 19, 2008

2. Date for delivery of rebuttal expert reports: February 20, 2009

3. Expert discovery shall be completed by: April 3, 2009

4. Dispositive motions shall be filed by: April 13, 2009

5. Plaintiff reserves the right to respond to opinions contained in Defendants' rebuttal report on secondary considerations.

CONSENTED TO BY:

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Attorneys for Defendant Sun Pharmaceutical Industries Ltd.

SO ORDERED:

Dated: 11/20/09

Honorable Mark Falk, U.S.M.J.

EXHIBIT E

UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

JAZZ PHARMACEUTICALS, INC., **Plaintiff,** **v.** **ROXANE LABORATORIES, INC.,** **Defendant.**	**Civil Action No. 10-6108 (SDW)(MCA)** **Hon. Susan D Wigenton, U.S.D.J.** **Hon. Madeline C. Arleo, U.S.M.J.** **[PROPOSED] PRETRIAL SCHEDULING ORDER**

THIS MATTER having come before the Court for a telephonic status conference on June 6, 2011; and for good cause shown:

IT IS on this ___ day of June, 2011,

ORDERED THAT:

DISCOVERY AND MOTION PRACTICE

		PROPOSED DATES
1.	Defendant serves non-infringement and invalidity contentions	April 14, 2011
2.	Plaintiff serves infringement contentions and identifies asserted claims	June 1, 2011
3.	Parties exchange proposed terms for construction and thereafter meet and confer to narrow issues	July 8, 2011

4.	Parties exchange preliminary proposed constructions and identifications of intrinsic and extrinsic evidence and thereafter meet and confer to narrow issues	August 1, 2011
5.	Parties file Joint Claim Construction and Pre-hearing Statement	August 26, 2011
6.	Parties complete fact discovery related to claim construction	September 23, 2011
7.	Parties file opening Markman papers, including any expert declarations	October 19, 2011
8.	Deadline for motions to amend pleadings or add parties	December 5, 2011
9.	Parties complete expert discovery regarding Markman issues	November 18, 2011
10.	Parties file responsive Markman papers, including any responding expert declarations	December 19, 2011
11.	Parties propose schedule to the Court for Claim Construction Hearing	December 30, 2011
12.	Close of fact discovery	February 22, 2012
13.	Opening expert reports on issues for which the party bears the burden of proof	April 20, 2012
14.	Opposition expert reports	May 25, 2012
15.	Rebuttal expert reports	June 27, 2012

16.	Close of expert discovery	August 22, 2012
17.	Final pretrial conference	October 22, 2012, or any date as is convenient for the Court
18.	Trial	December 10, 2012, or any other date as is convenient for the Court

MADELINE COX ARLEO
United States Magistrate Judge

Original: Clerk of the Court
cc: All Parties
Deputy Clerk
File